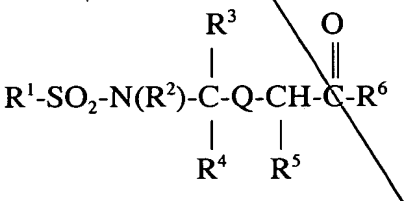
R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R^5 is selected from the group consisting of isopropyl, $-CH_2X$ and $=CH-X$ where X is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic with the proviso that when R^5 is $=CH-X$ then (H) is removed from the formula and X is not hydroxyl;

Q is $-C(X)NR^7-$ wherein R^7 is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur;

or pharmaceutically acceptable salts thereof.

2. (Amended) A compound of formula IA below:



IA

where

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^2 and R^3 together with the nitrogen atom bound to R^2 and the carbon atom bound to R^3 form a heterocyclic or a substituted heterocyclic group;

R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R^5 is selected from the group consisting of isopropyl, $-CH_2X$ and $=CH-X$ where X is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic with the proviso that when R^5 is $=CH-X$ then (H) is removed from the formula and X is not hydroxyl;

R^6 is selected from the group consisting of amino, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, -O-(N-succinimidyl), -NH-adamantyl, -O-cholest-5-en-3-β-yl, -NHOY where Y is hydrogen, alkyl, substituted alkyl, aryl, or substituted aryl, $-NH(CH_2)_pCOOY$ where *p* is an integer of from 1 to 8 and Y is as defined above, $-OCH_2NR^9R^{10}$ where R^9 is selected from the group consisting of -C(O)-aryl and -C(O)-substituted aryl and R^{10} is selected from the group consisting of hydrogen and $-CH_2COOR^{11}$ where R^{11} is alkyl, and $-NHSO_2Z$ where Z is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic or substituted heterocyclic;

Q is $-C(X)NR^7-$ wherein R^7 is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur;

or pharmaceutically acceptable salts thereof

with the proviso that

when R^1 is *p*-methylphenyl, R^2 and R^3 are joined together with the nitrogen atom pendent to R^2 and the carbon atom pendent to R^3 to form a pyrrolidinyl ring, R^4 is methyl, R^5 is *p*-hydroxybenzyl then R^6 is not *t*-butoxy.

Cancel Claims 5-6 without prejudice.

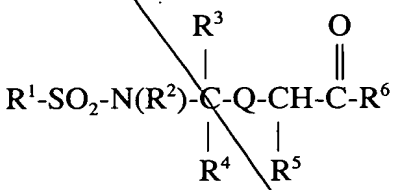
A4

7. (Amended) The compound according to Claims 1 or 2 wherein R^2 and R^3 together with the nitrogen atom bound to R^2 substituent and the carbon bound to the R^3 substituent form a substituted heterocyclic ring.

Cancel Claims 8-9, 11 and 14 without prejudice.

A5

16. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of the formula:



where

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocylic, heteroaryl and substituted heteroaryl;

R^2 and R^3 together with the nitrogen atom bound to R^2 and the carbon atom bound to R^3 form a heterocyclic or a substituted heterocyclic group;

R^4 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R^5 is selected from the group consisting of isopropyl, $-CH_2X$ and $=CH-X$ where X is selected from the group consisting of hydrogen, hydroxyl, acylamino, alkyl, alkoxy, aryloxy, aryl, aryloxyaryl, carboxyl, carboxylalkyl, carboxyl-substituted alkyl, carboxyl-cycloalkyl, carboxyl-substituted cycloalkyl, carboxylaryl, carboxyl-substituted aryl, carboxylheteroaryl, carboxyl-substituted heteroaryl, carboxylheterocyclic, carboxyl-substituted heterocyclic, cycloalkyl, substituted alkyl, substituted alkoxy, substituted aryl, substituted aryloxy, substituted aryloxyaryl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic with the proviso that when R^5 is

=CH-X then (H) is removed from the formula and X is not hydroxyl;

R^6 is selected from the group consisting of 2,4-dioxo-tetrahydrofuran-3-yl (3,4-enol), hydroxyl, amino, alkoxy, substituted alkoxy, cycloalkoxy, substituted cycloalkoxy, -O-(N-succinimidyl), -NH-adamantyl, -O-cholest-5-en-3-β-yl, -NHOY where Y is hydrogen, alkyl, substituted alkyl, aryl, or substituted aryl, $-NH(CH_2)_pCOOY$ where *p* is an integer of from 1 to 8 and Y is as defined above, $-OCH_2NR^9R^{10}$ where R^9 is selected from the group consisting of -C(O)-aryl and -C(O)-substituted aryl and R^{10} is selected from the group consisting of hydrogen and $-CH_2COOR^{11}$ where R^{11} is alkyl, and $-NHSO_2Z$ where Z is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic or substituted heterocyclic;

Q is $-C(X)NR^7-$ wherein R^7 is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur;

or pharmaceutically acceptable salts thereof

with the proviso that

when R^1 is *p*-methylphenyl, R^2 and R^3 are joined together with the nitrogen atom pendent to R^2 and the carbon atom pendent to R^3 to form a pyrrolidinyl ring, R^4 is methyl, R^5 is *p*-hydroxybenzyl then R^6 is not *t*-butoxy.

18. (Amended) The method according to Claim 17 wherein said inflammatory disease is selected from the group consisting of asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, tissue transplantation, tumor metastasis, meningitis, encephalitis, cerebral traumas, nephritis, retinitis, atopic dermatitis, psoriasis, myocardial ischemia and acute leukocyte-mediated lung injury such as that which occurs in adult respiratory distress syndrome.

19. (New) The method according to Claim 18 wherein said diabetes is acute juvenile onset diabetes.

20. (New) The method according to Claim 18 wherein said inflammatory bowel disease is ulcerative colitis or Crohn's disease.

21. (New) The method according to Claim 18 wherein said cerebral trauma is stroke.

22. (New) A compound selected from the group consisting of:

N-(toluene-4-sulfonyl)-L-α-methylprolyl-L-phenylalanine;

N-(toluene-4-sulfonyl)-L-α-methylprolyl-L-4-(isonicotinamido)phenylalanine methyl ester;

N-(toluene-4-sulfonyl)-L-α-methylprolyl-L-4-(isonicotinamido)phenylalanine;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(1-methylpiperidin-4-oxy)phenylalanine ethyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(1-methylpiperidin-4-oxy)phenylalanine;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(4-methylpiperazin-1-carbonyloxy)phenyl-alanine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(*N*,*N*-dimethylcarbamyloxy)phenyl-alanine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(4-methylpiperazin-1-carbonyloxy)phenyl-alanine;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-tyrosine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(*N*,*N*-dimethylcarbamyloxy)phenylalanine;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(morpholin-4-ylcarbonyloxy)phenyl-alanine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(morpholin-4-ylcarbonyloxy)phenyl-alanine;

N-(toluene-4-sulfonyl)-α-methylprolyl-D-tyrosine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-(morpholin-4-ylcarbonyloxy)phenyl-alanine 1-(trimethyacetoxy)methyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-[N-(2-(N',N'-dimethylamino)ethyl)-N-methylcarbamyloxy]phenylalanine *tert*-butyl ester;

N-(toluene-4-sulfonyl)-α-methylprolyl-L-4-[N-(2-(N',N'-dimethylamino)ethyl)-N-methylcarbamyloxy]phenylalanine;

N-(4-fluorobenzenesulfonyl)-α-methylprolyl-L-4-(*N*,*N*-dimethylcarbamyloxy)phenyl-alanine *tert*-butyl ester;

N-(4-fluorobenzenesulfonyl)-α-methylprolyl-L-4-(*N*,*N*-dimethylcarbamyloxy)phenyl-alanine

or pharmaceutically acceptable salts thereof as well as any of the ester compounds recited above wherein one ester group is replaced with another ester group selected from the group consisting of methyl ester, ethyl ester, *n*-propyl ester, isopropyl ester, *n*-butyl ester, isobutyl ester, *sec*-butyl ester and *tert*-butyl ester.

REMARKS

Claim Status

Applicants respectfully request that the instant application be reconsidered in view of the above amendments and the following remarks. Claims 1-18 were pending in the application. Of these claims, the Examiner withdrew from consideration claims 5, 8, 9 and 11. Applicants request the cancellation of claims 5-6, 8-9, 11 and 14 and reserve the right to file applications directed to the canceled subject matter at a later date. Applicants further request the addition of claims 19-22. Upon entry of this Amendment, claims 1-4, 7, 12, 13, and 15-22 will be pending in the instant application.

Election/Restriction

Applicants respectfully acknowledge the Examiner's amendment of Group III to contain claims 1-4, 6-7, 10 and 12-18.